

2/40

LUV-SUV #2		Hepatic mRNA content (pg/ug)							
Rabbit #	Treatment	CETP	HMG-CoA R	LDL R	7a-hydroxylase	LDL ChE, day 1	LDL ChE, day 3	LDL ChE, day 5	LDL ChE, day 6
1	(A) PBS	2.87	0.54	4.27	0.56	7.4	7.1	5.2	6.5
2	(A) PBS	5.63	0.55	5.38	0.39	18.1	11.8	6.2	9.7
3	(A) PBS	5.34	0.39	8.93	0.74	8.5	8.9	4.4	8.7
4	(A) PBS	5.04	0.55	5.49	0.82	14.1	14.1	6.8	8.6
	Mean	4.72	0.51	6.02	0.83	11.53	10.48	6.15	8.38
	SEM	0.63	0.04	1.01	0.10	2.12	1.55	0.98	0.67
5	(B) LUV	3.15	0.58	7.23	0.63	25.3	14.9	13.6	10.5
6	(B) LUV	3.02	0.47	8.15	0.58	14.0	15.9	10.8	8.2
7	(B) LUV	2.52	0.58	4.81	0.83	28.3	22.5	21.3	22.4
8	(B) LUV	2.68	0.58	7.37	0.94	17.5	21.8	13.4	9.5
	Mean	2.84	0.55	8.69	0.75	21.28	16.78	14.78	12.85
	SEM	0.15	0.03	0.72	0.08	3.33	1.96	2.27	3.28
	t vs. PBS	2.910	0.939	0.703	0.919	2.473	3.318	3.506	1.275
13	SUV + LUV	3.18	0.50	5.28	0.51	11.9	34.0	20.1	22.2
10	(C) SUV	5.64	0.38	3.98	0.30	21.1	45.3	15.3	46.3
11	(C) SUV	3.39	0.29	3.67	0.42	10.0	36.3	59.6	42.7
12	(C) SUV	3.00	0.13	3.34	0.63	17.8	31.8	45.5	22.3
	Mean w/o #13	4.01	0.27	3.66	0.45	16.30	37.80	40.13	37.10
	SEM w/o #13	0.02	0.07	0.18	0.10	3.28	3.97	13.07	7.47
	t vs. PBS	0.686	2.903	2.295	1.304	1.220	6.414	2.594	3.628
	t vs. LUV	1.397	3.660	4.328	2.301	1.963	4.296	1.912	2.98
	Mean w/ #13	3.80	0.33	4.07	0.47	15.20	38.86	35.13	33.38
	SEM w/ #13	0.62	0.06	0.42	0.07	2.57	2.96	10.51	8.48
	t vs. PBS	1.041	2.091	1.781	1.369	1.103	7.890	2.748	3.848
	t vs. LUV	1.512	2.763	3.369	2.554	1.445	8.085	1.893	2.856

FIG. 2

3/40

Plasma LDL cholesteryl ester concentrations  
in response to injections of LUVs, SUVs, or saline

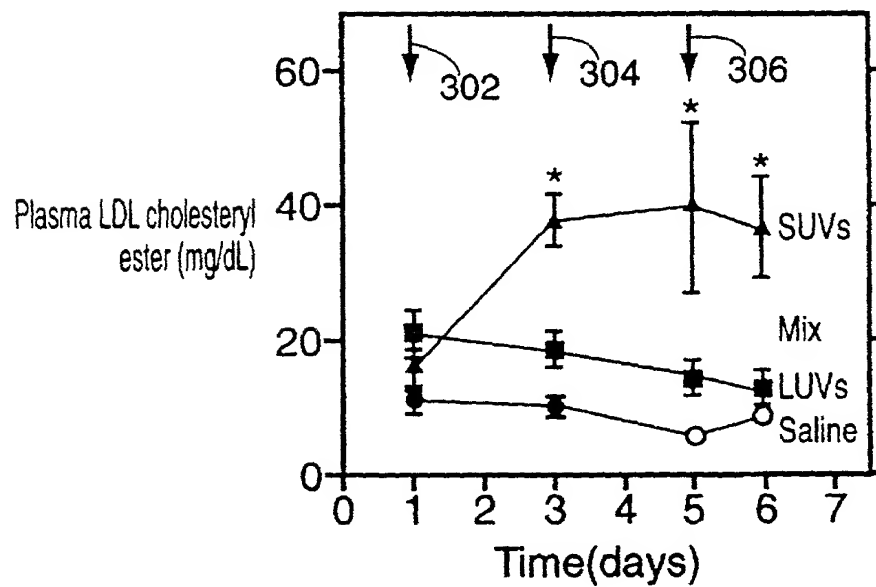
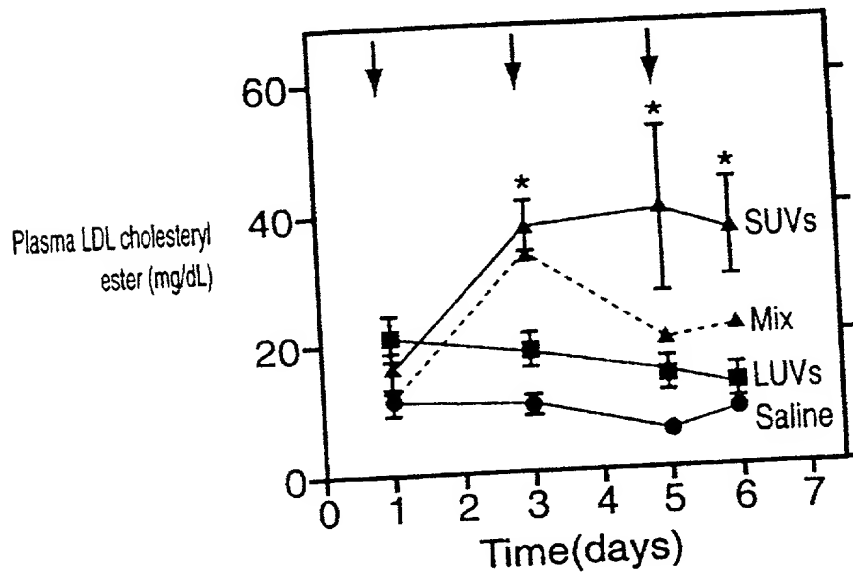


FIG. 3

4/40

Plasma LDL cholesteryl ester concentrations  
in response to injections of LUVs, SUVs, or saline



"Mix" received SUVs on days 1, 3 & 5,  
but also a dose of LUVs on day 3.  
All other animals received single injections  
on days 1, 3 & 5 (indicated by arrows).

FIG. 4

5/40

LDL receptor mRNA levels in liver in response  
to injections of LUVs, SUVs, or saline

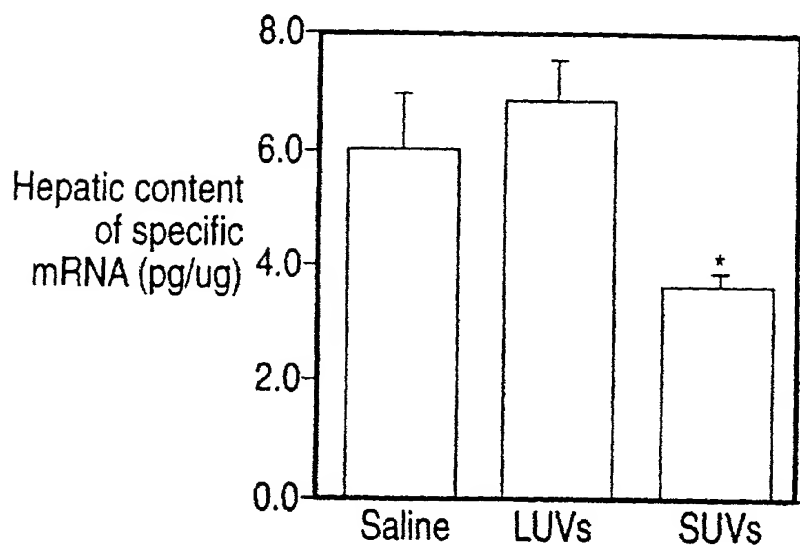


FIG. 5

6/40

LDL receptor mRNA levels in liver in response  
to injections of LUVs, SUVs, or saline

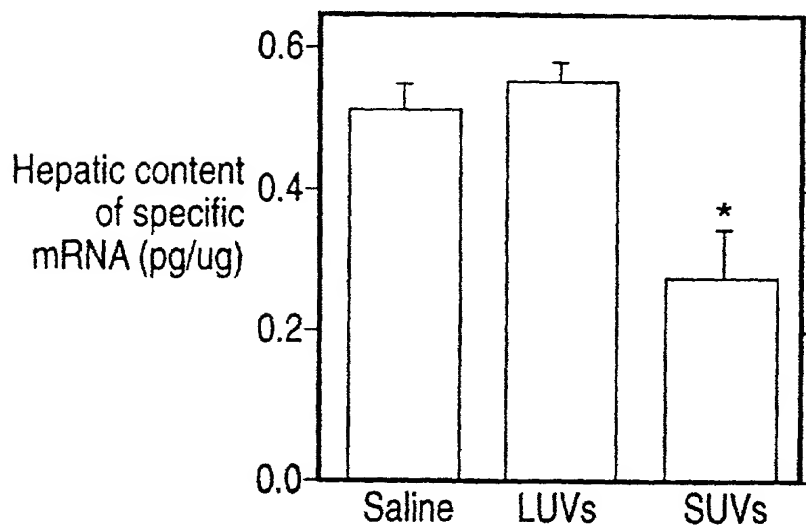


FIG. 6

7/40

Cholesteryl ester transfer protein mRNA levels in liver  
in response to injections of LUVs, SUVs, or saline

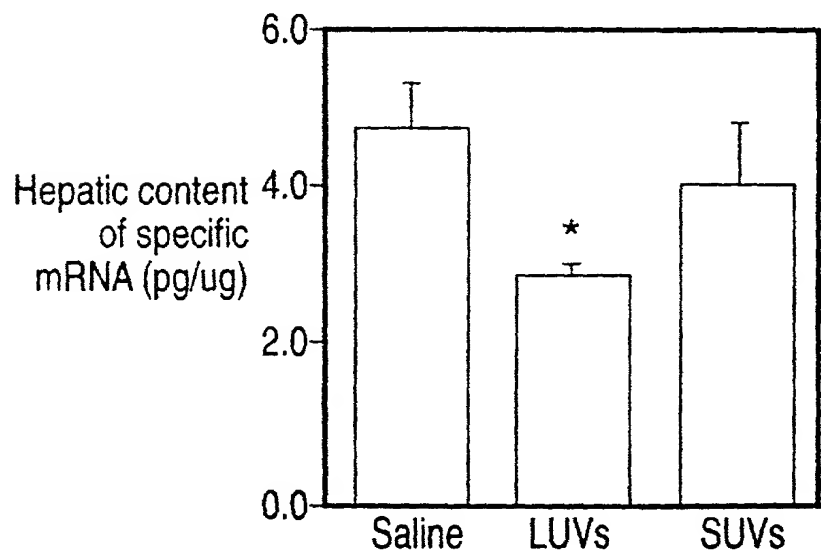


FIG. 7

8/40

7-alpha hydroxylase mRNA levels in liver in response  
to injections of LUVs, SUVs, or saline

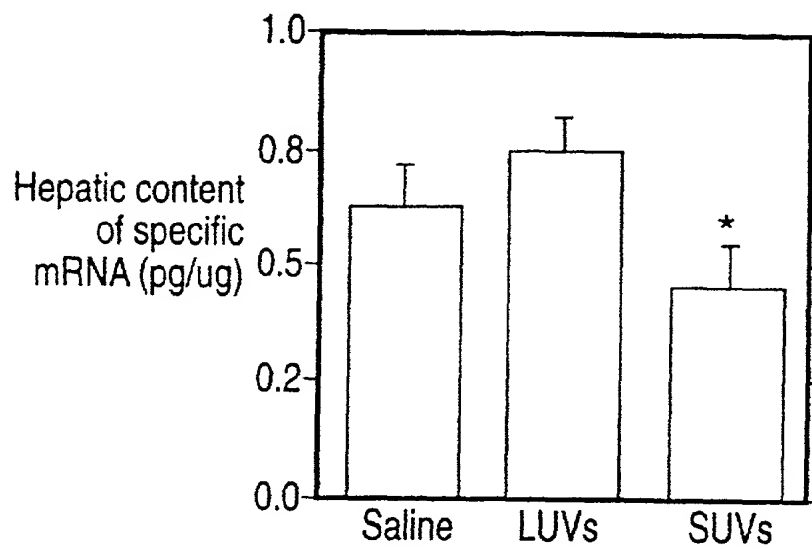


FIG. 8

\*Indicates column of interest



9/40

## Key points about LUV and atherosclerosis

1) Practical:     Straight forward to manufacture  
                      Non-toxic at very high doses

2) Mechanistic:     Liposomes promote reverse  
                             cholesterol transport *in vivo*

LUV are the optimal preparation

FIG. 9

10/40

Plasma unesterified cholesterol concentrations  
in response to injections of LUV, SUV, or saline

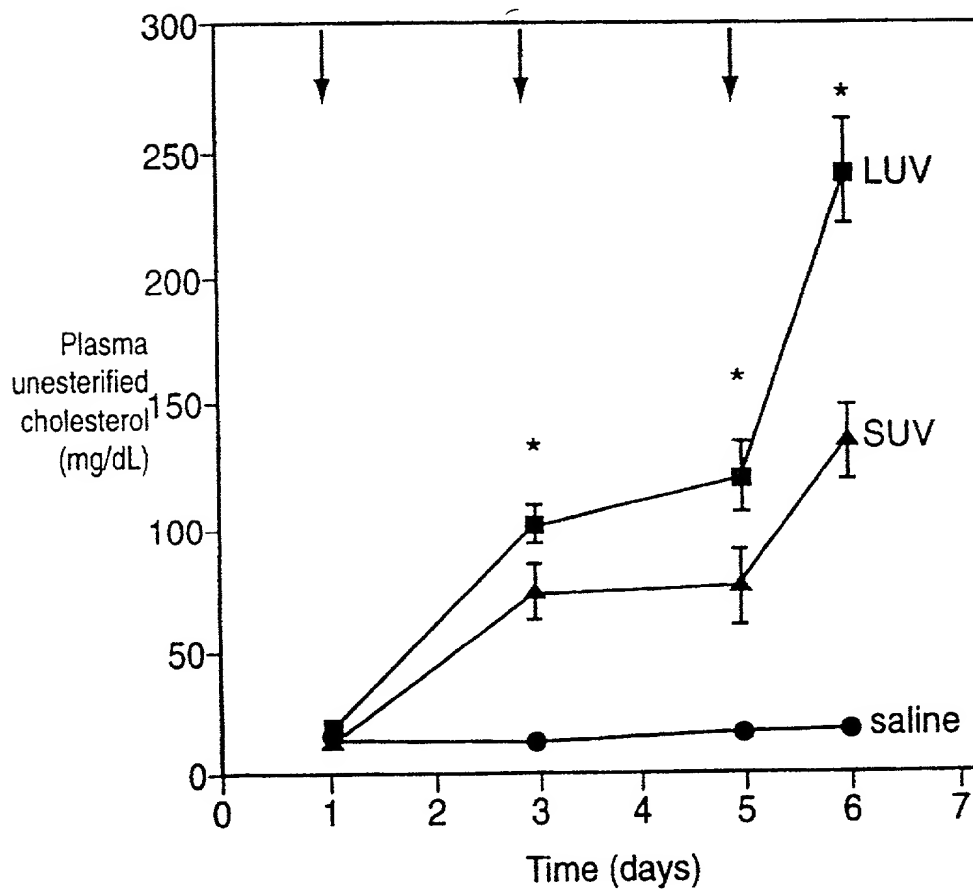


FIG. 10

11/40

Plasma esterified cholesterol concentrations  
in response to injections of LUV, SUV, or saline

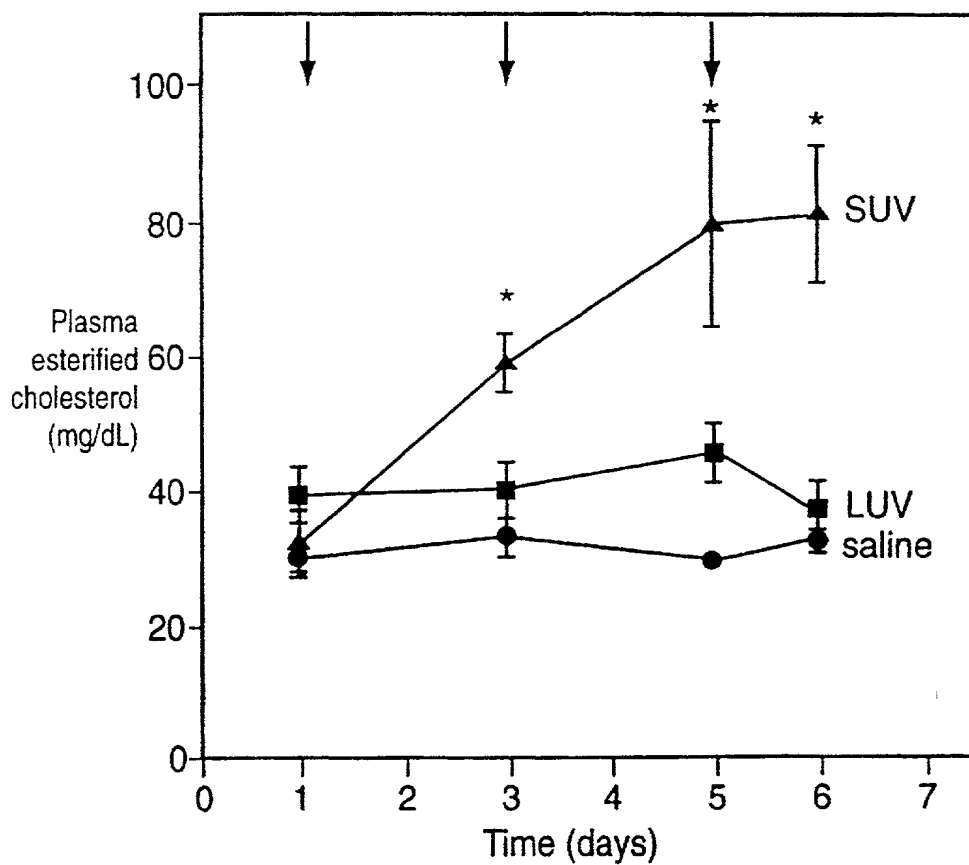


FIG. 11

12/40

LDL esterified cholesterol concentrations  
in response to injections of LUV, SUV, or saline

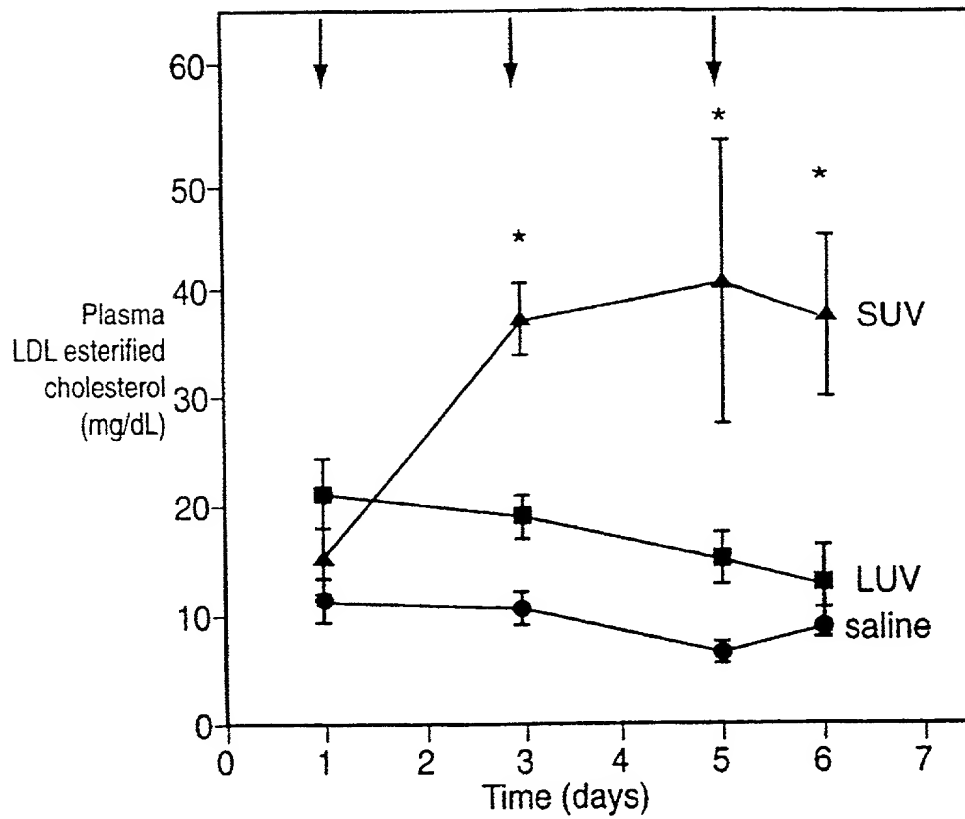


FIG. 12

13/40

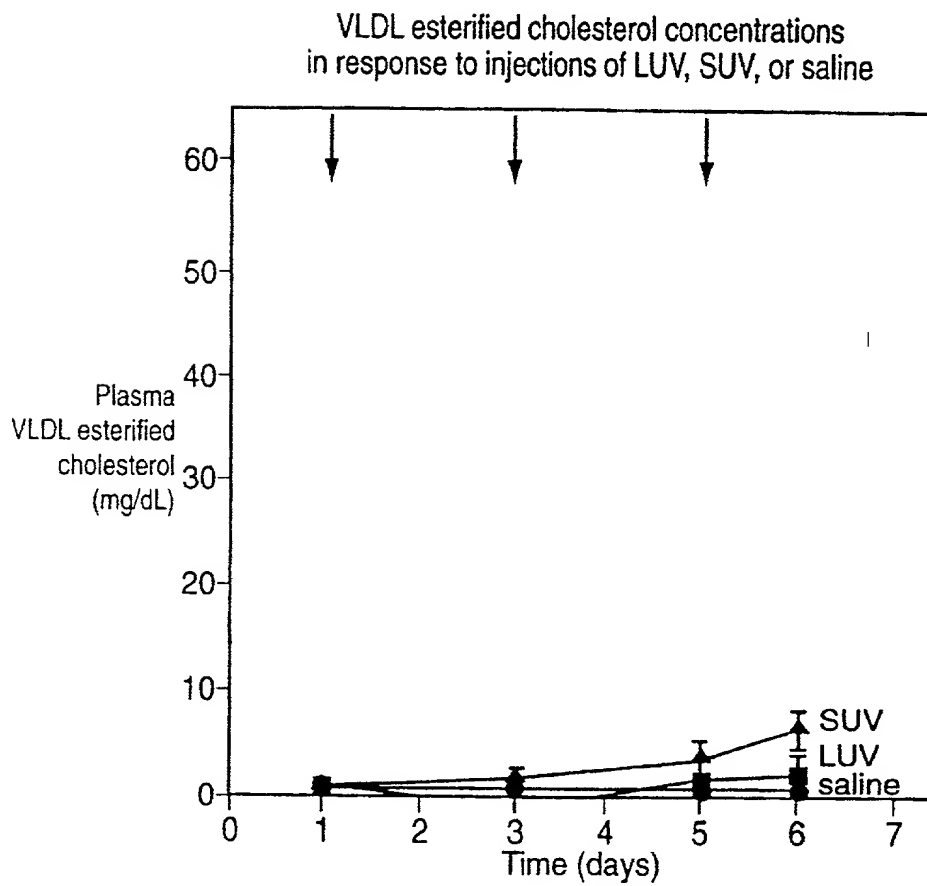


FIG. 13

14/40

HDL esterified cholesterol concentrations  
in response to injections of LUV, SUV, or saline

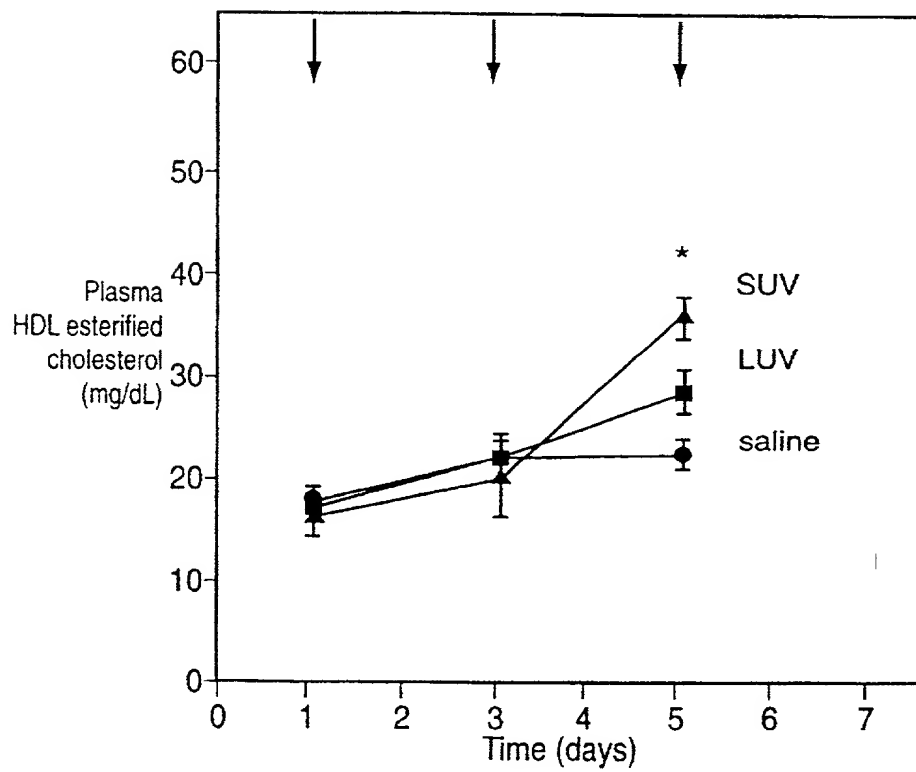


FIG. 14

15/40

HDL esterified cholesterol concentrations  
in response to injections of LUV, SUV, or saline

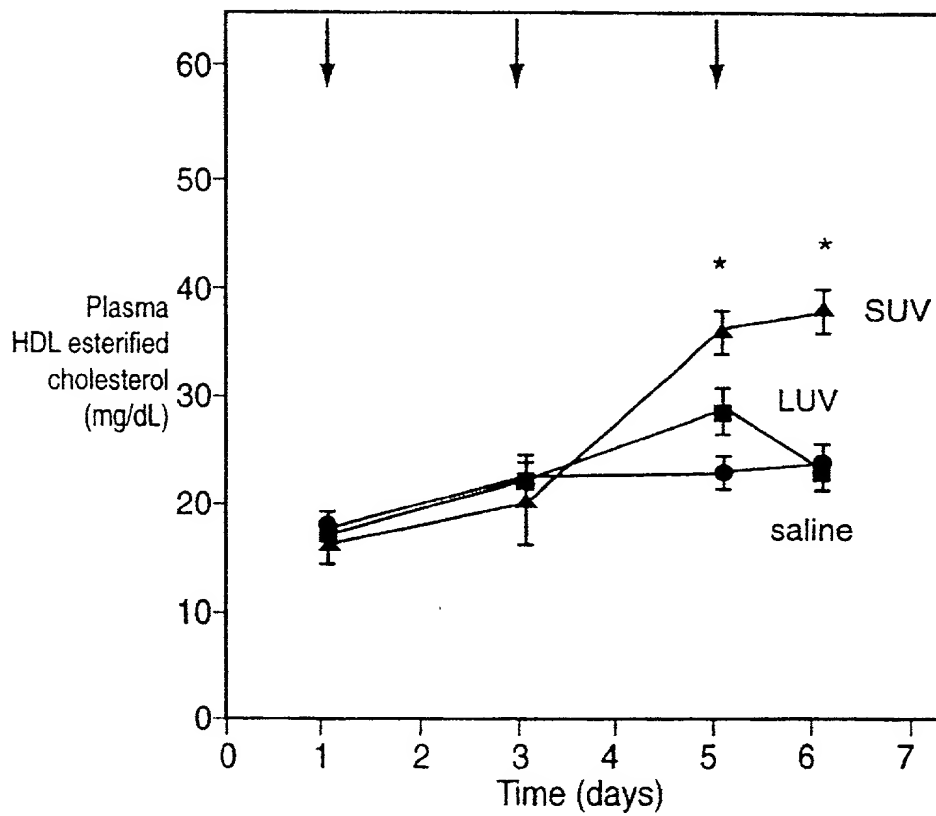


FIG. 15

16/40

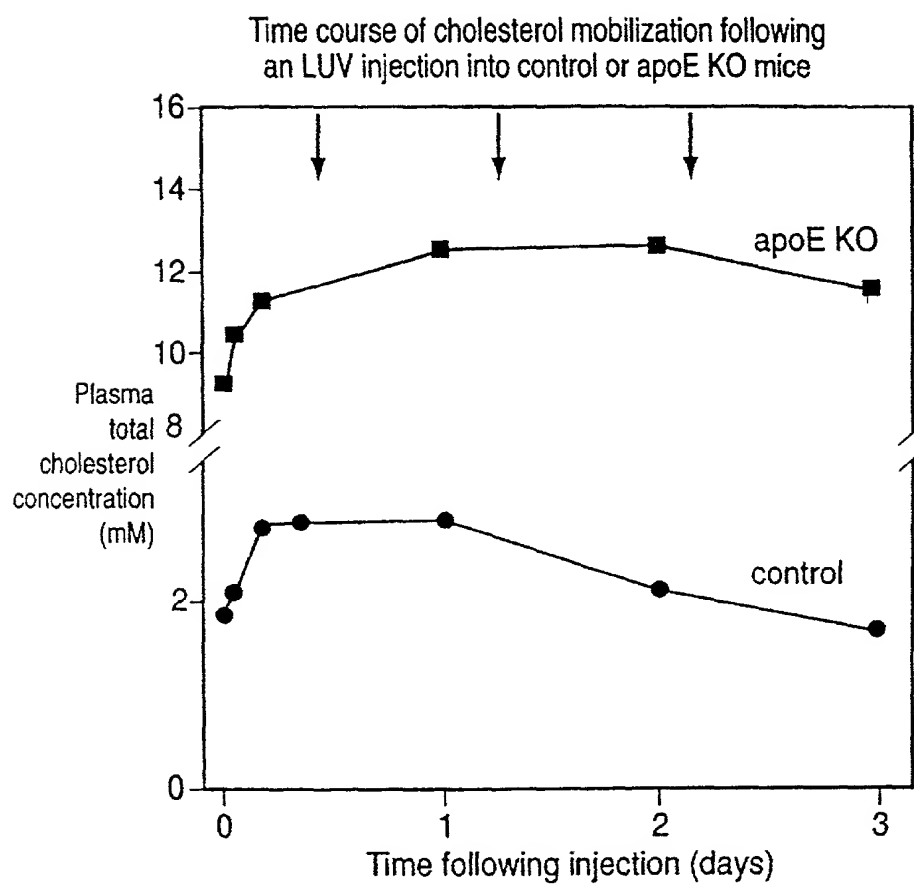


FIG. 16



17/40

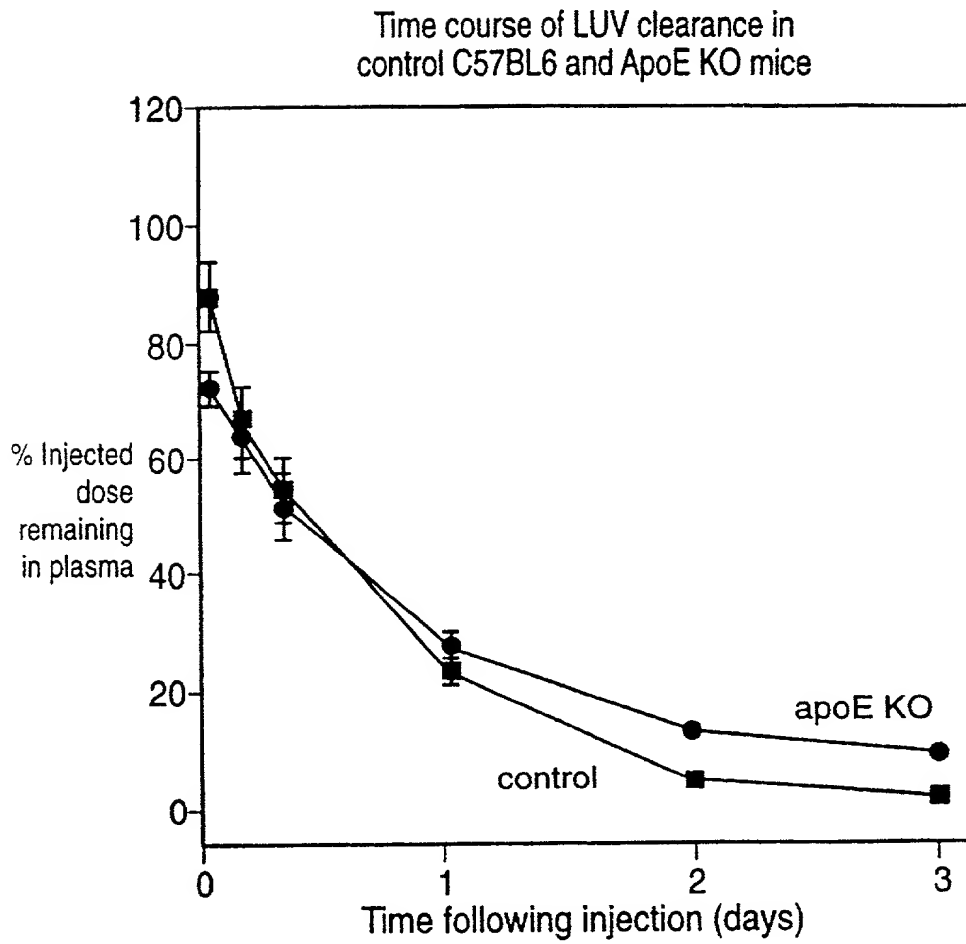


FIG. 17

18/40

- Effectiveness in humans

- Therapeutic targets

Lipid-rich, rupture-prone plaques  
Critical Stenosis  
Post-angioplasty re-stenosis  
Atherosclerosis in general

FIG. 18

19/40

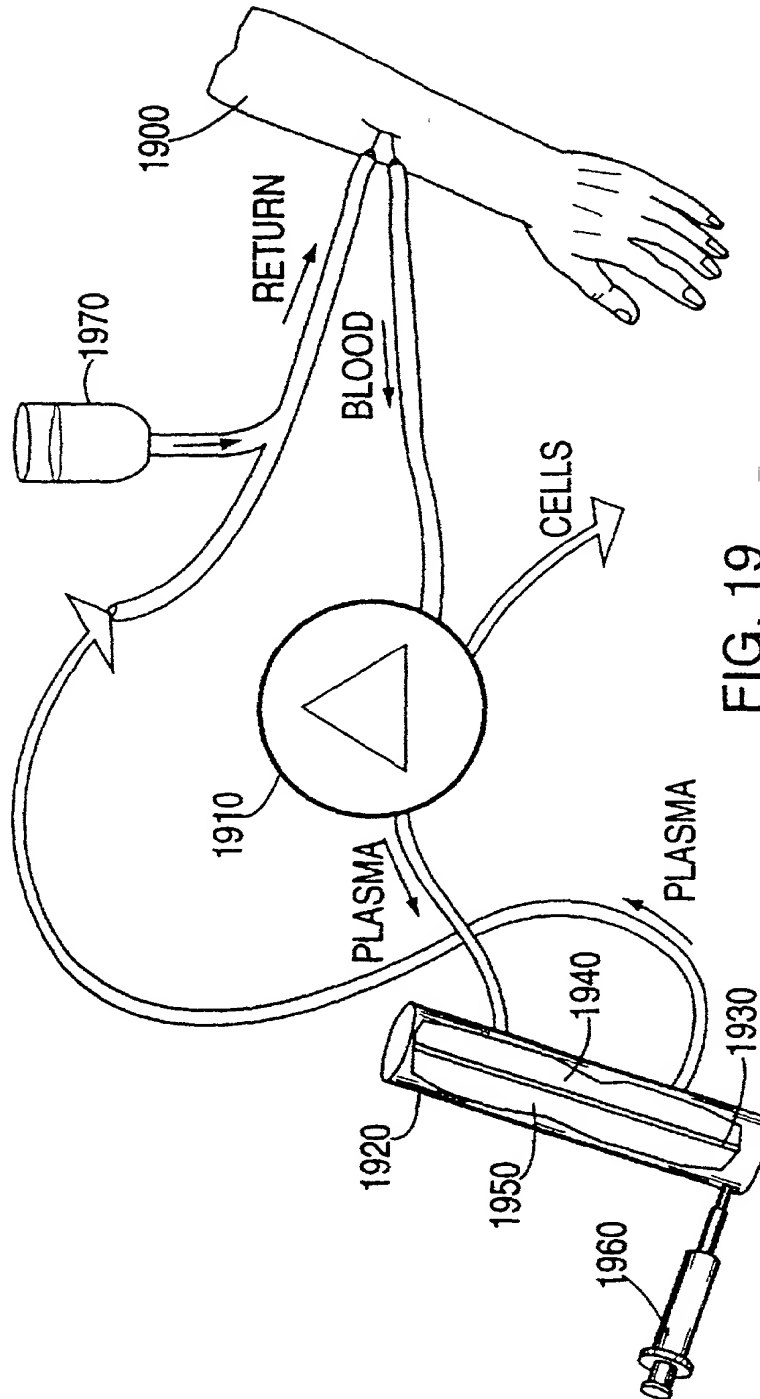


FIG. 19

FIG. 19

20/40

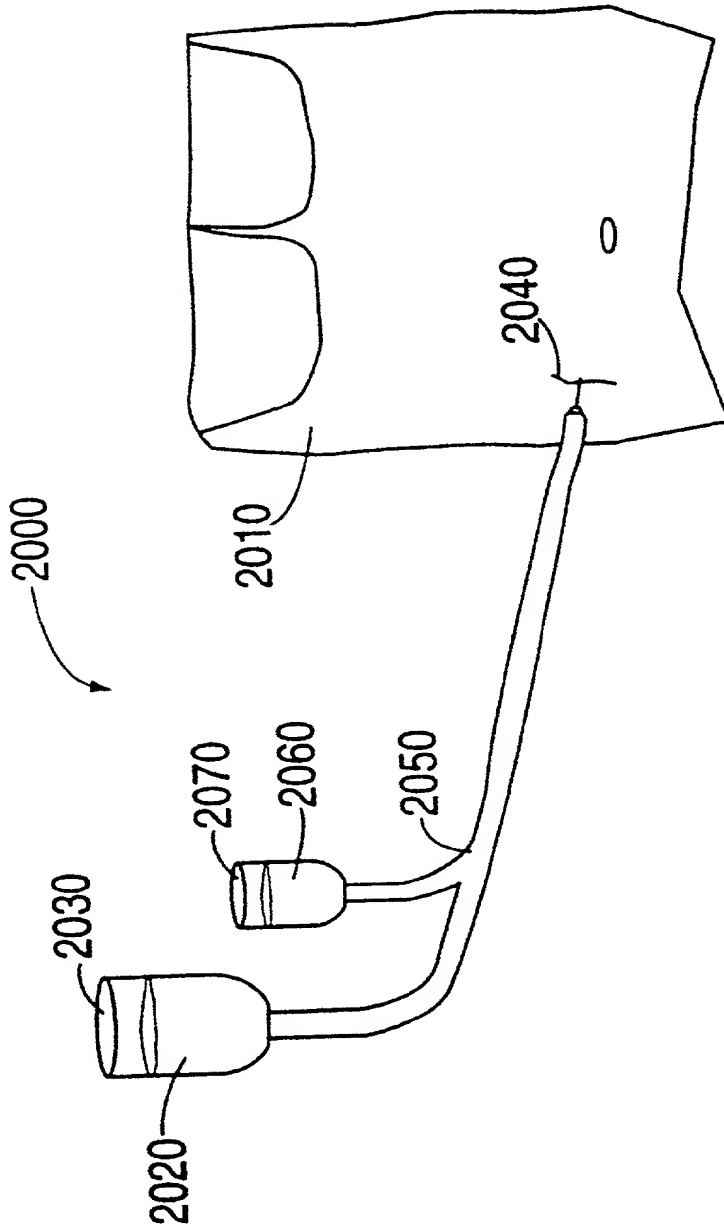


FIG. 20

21/40

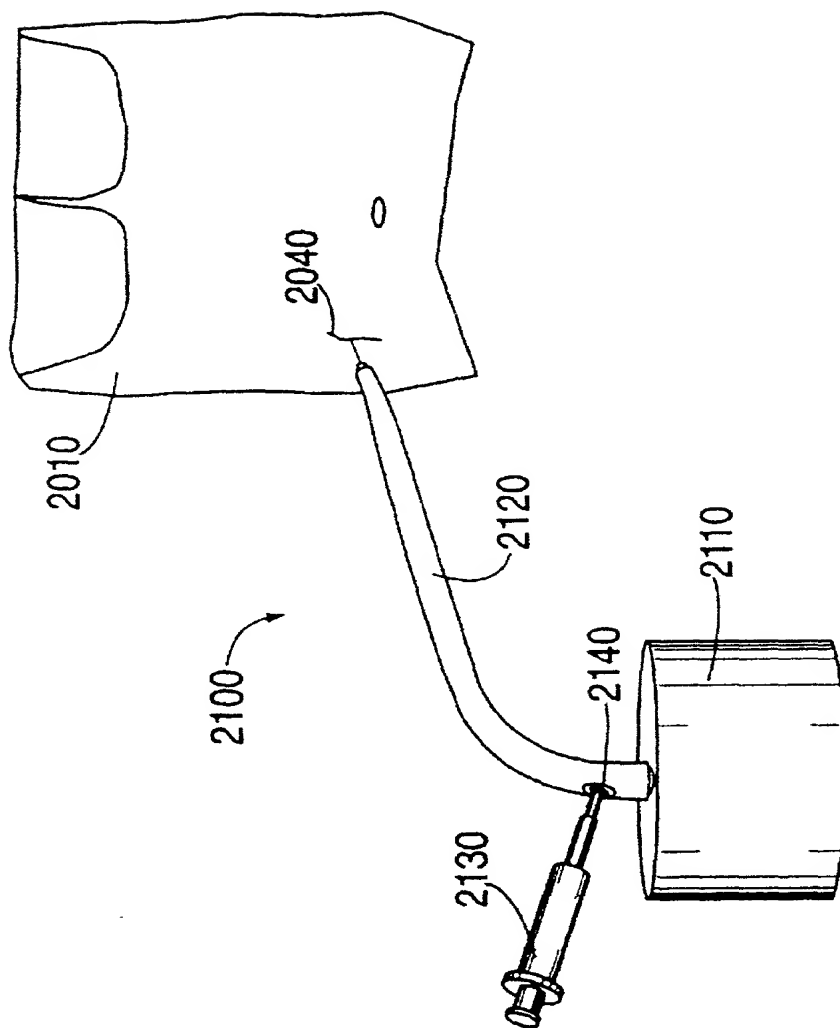


FIG. 21

FIG. 21

22/40

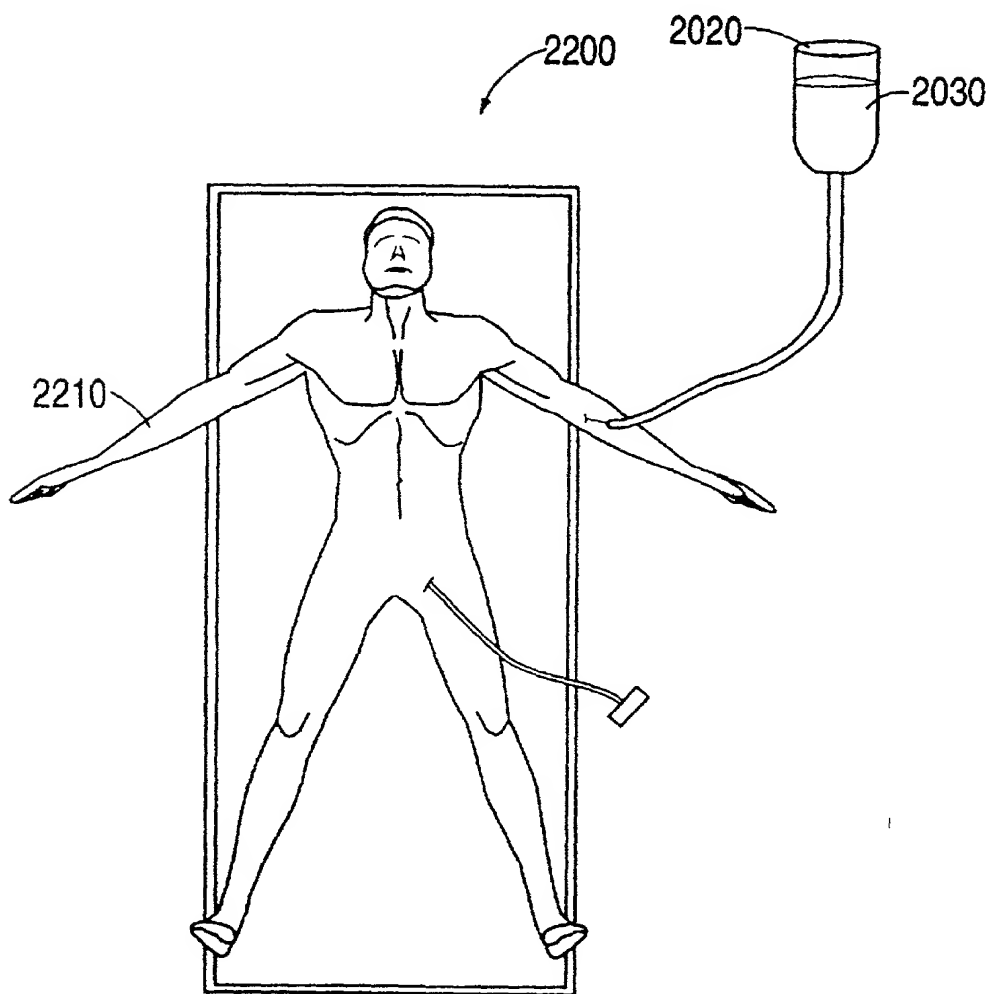


FIG. 22

23/40

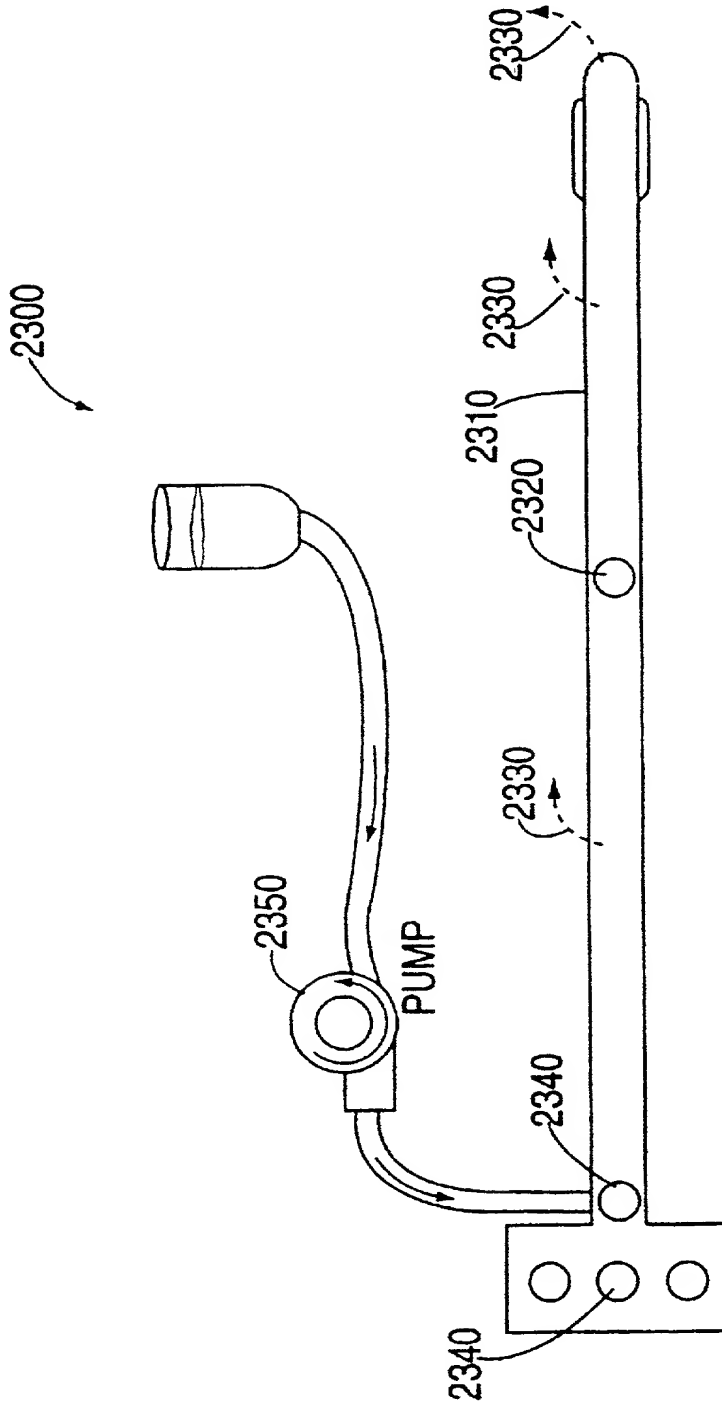


FIG. 23

24/40

Hepatic lipid contents in response to injections of LUVs, SUVs, or saline

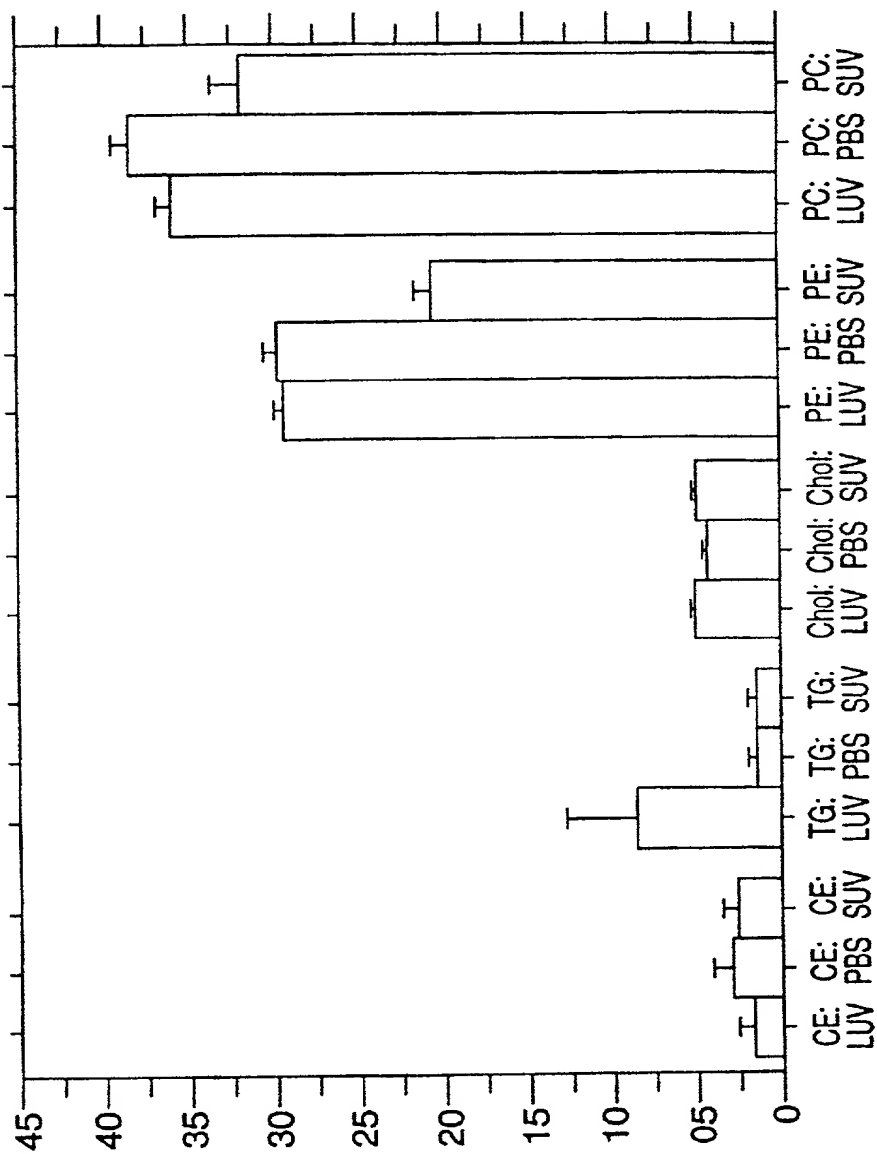


FIG. 24



25/40

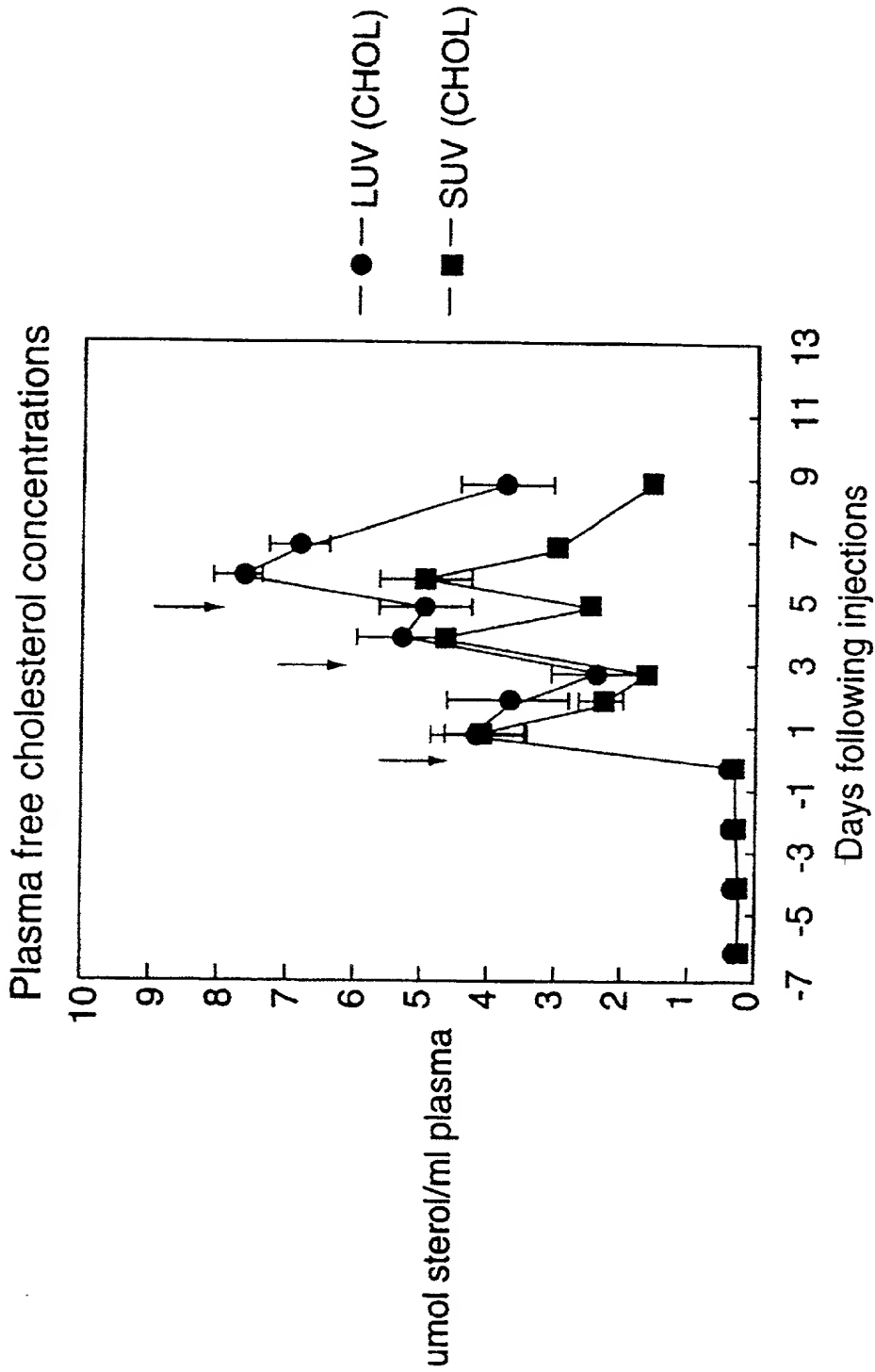


FIG. 25

26/40

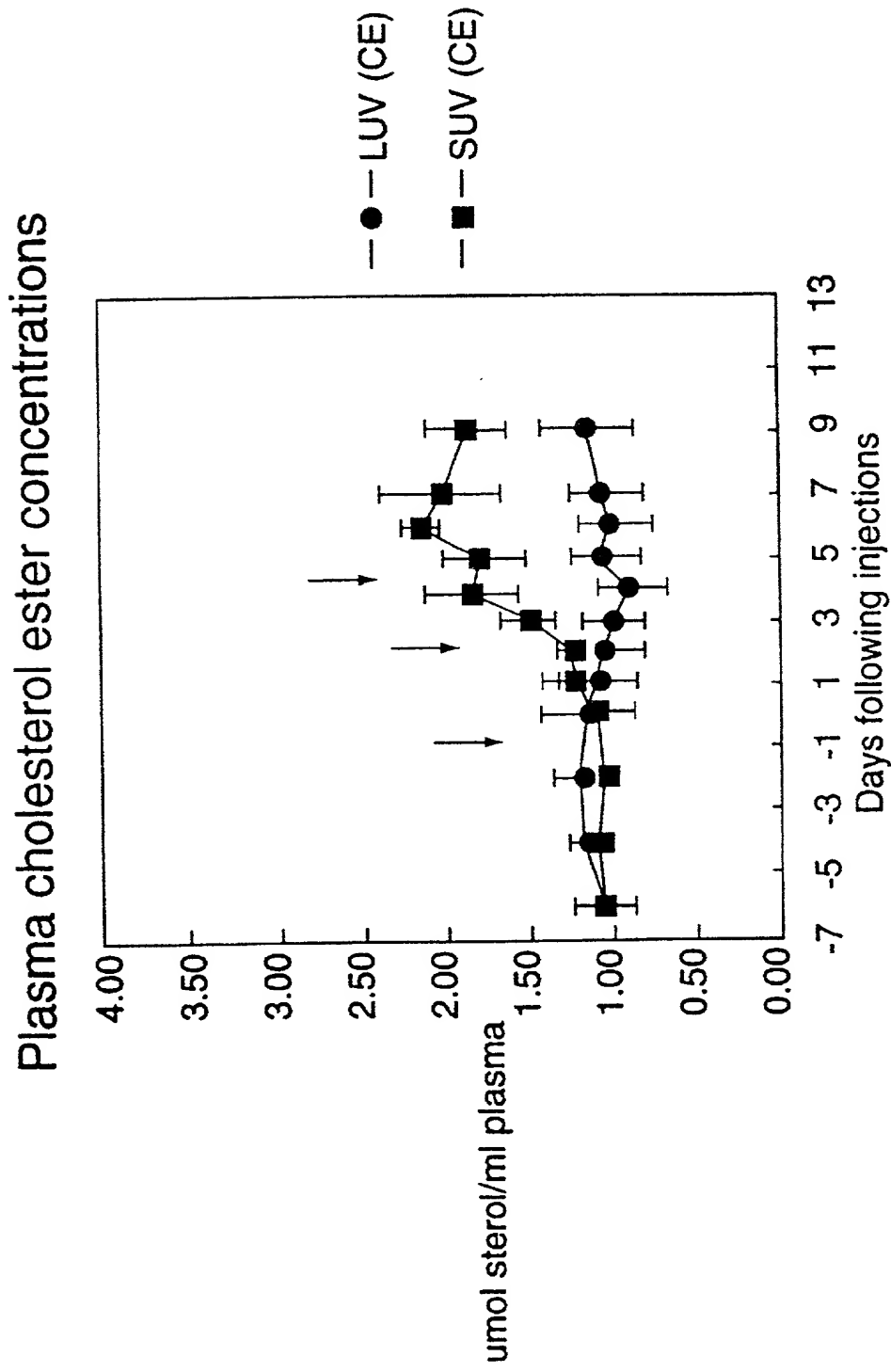


FIG. 26

27/40

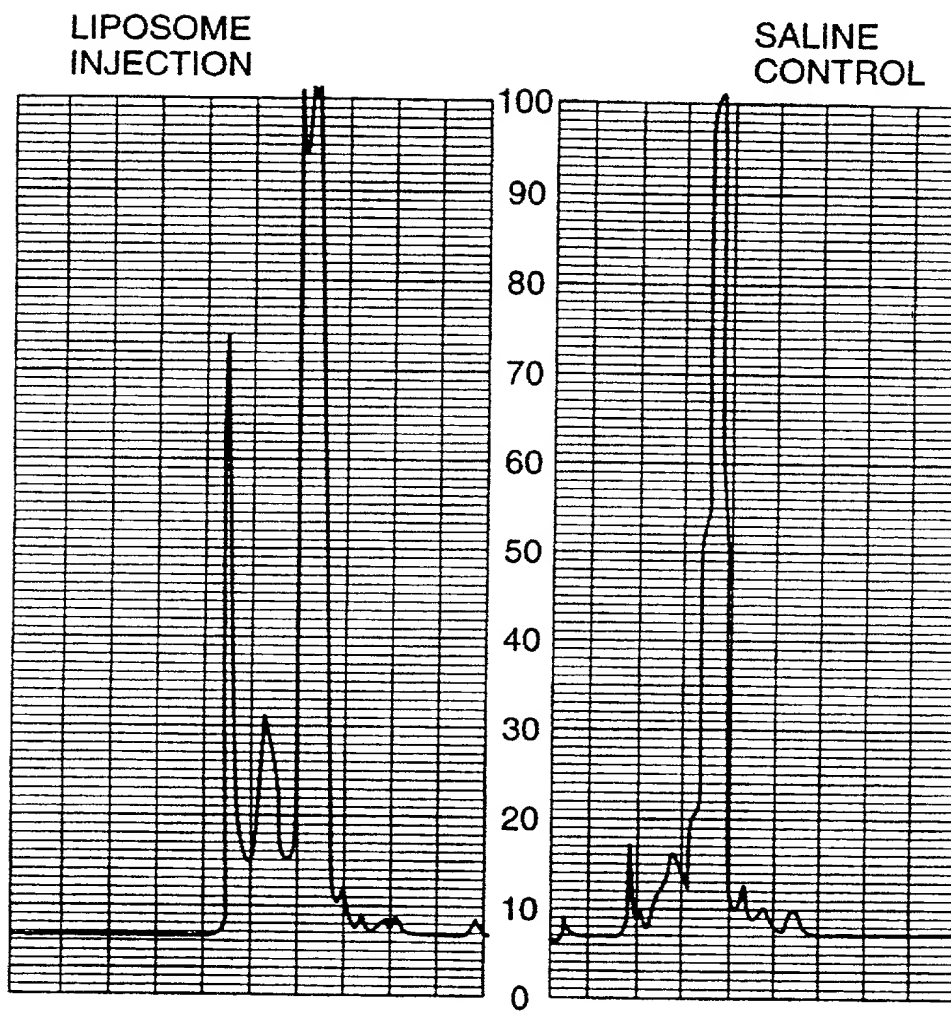


FIG. 27

28/40

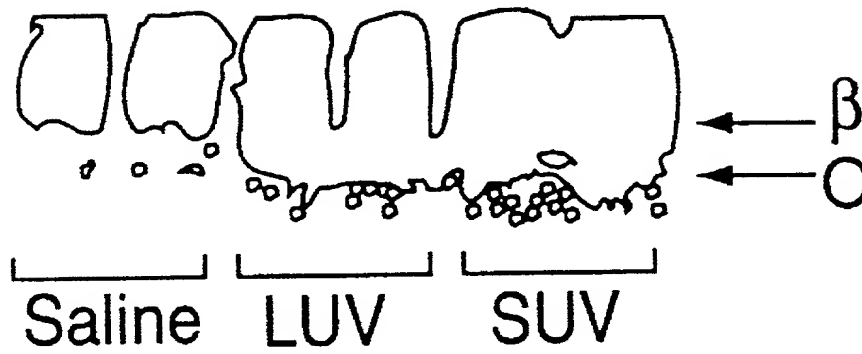


FIG. 28

29/40

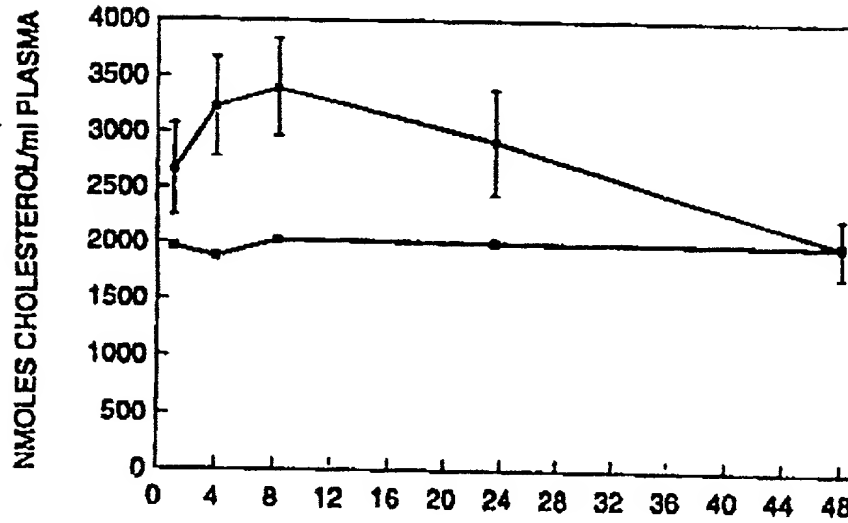


FIG. 29

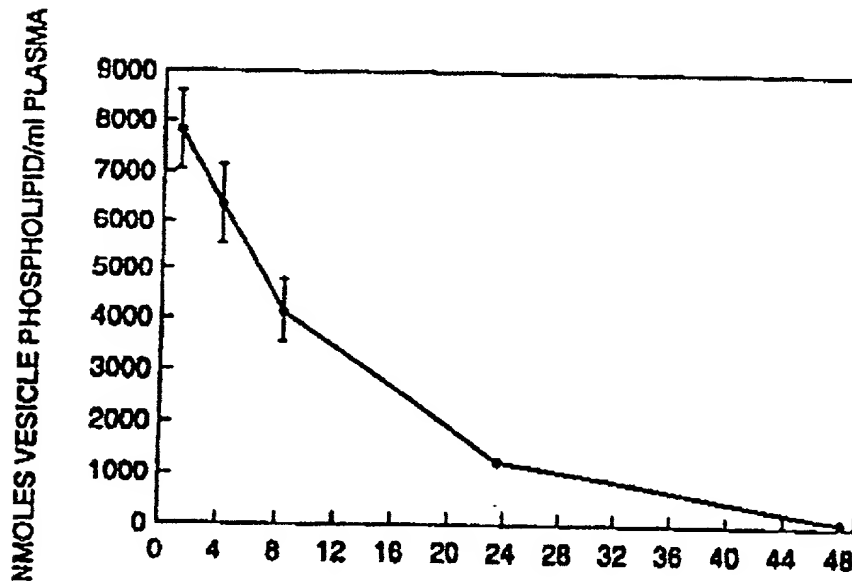


FIG. 30

30/40

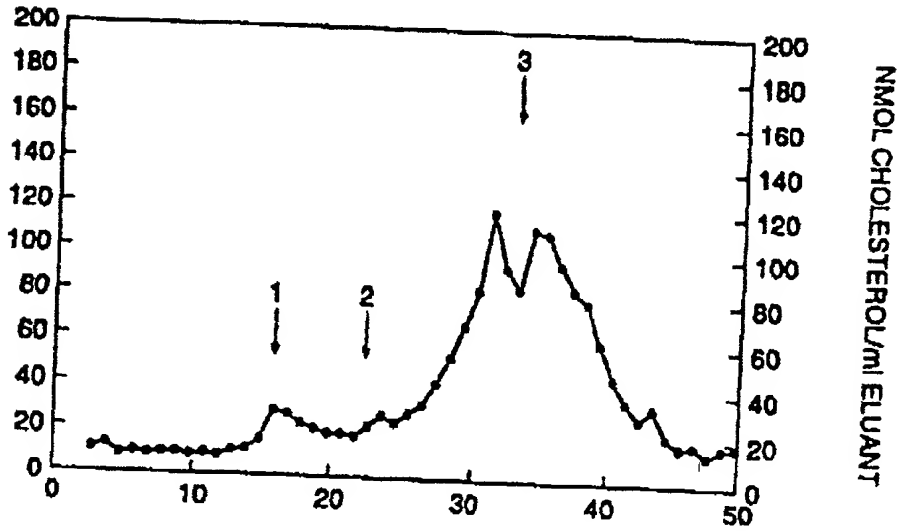


FIG. 31

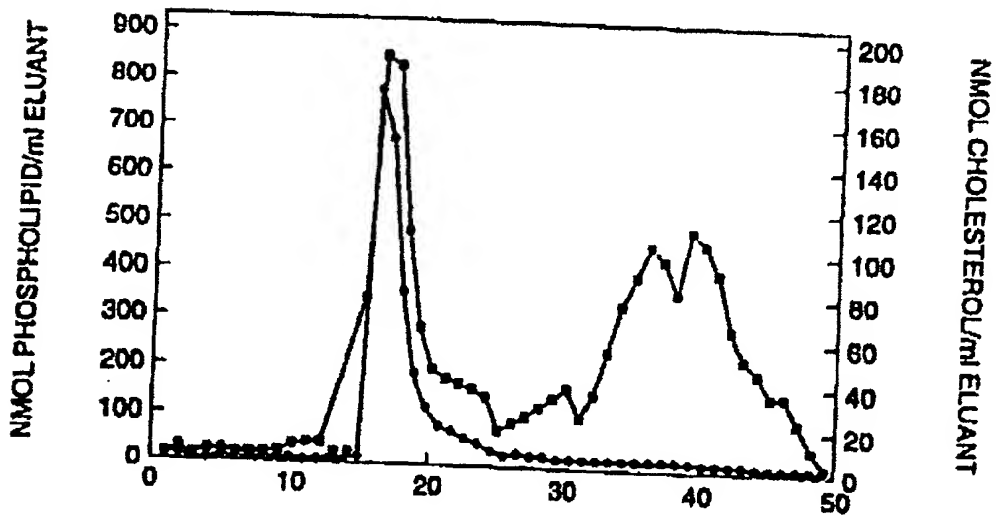


FIG. 32

31/40

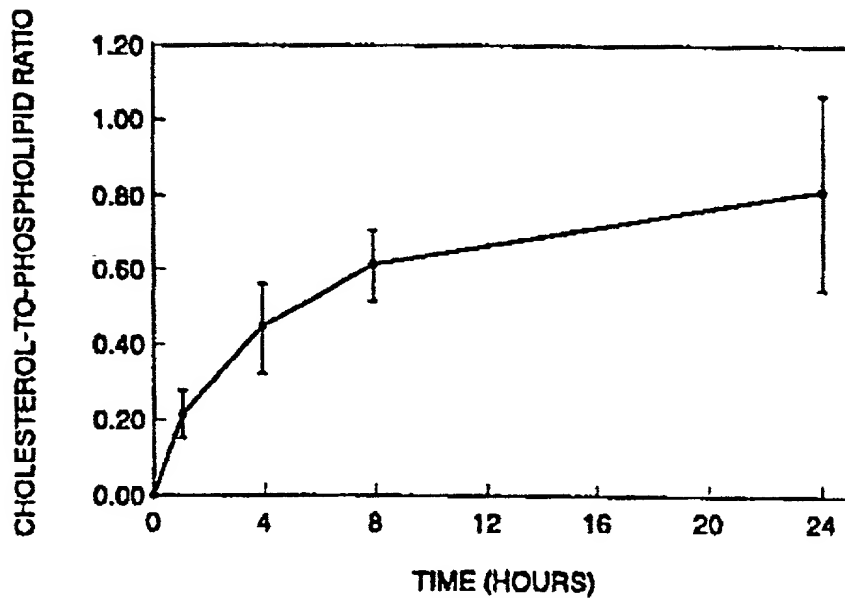


FIG. 33

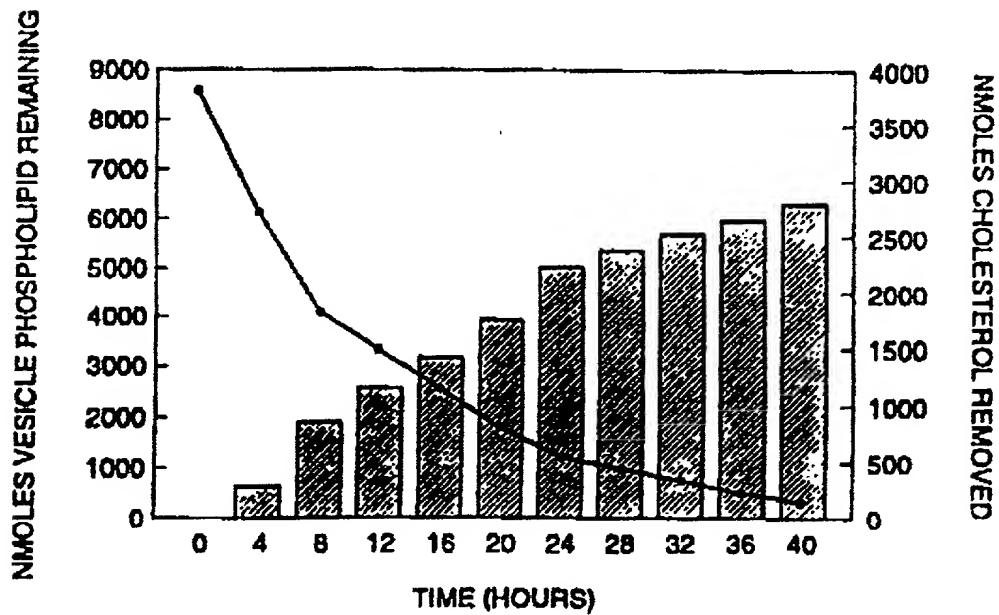


FIG. 34

32/40

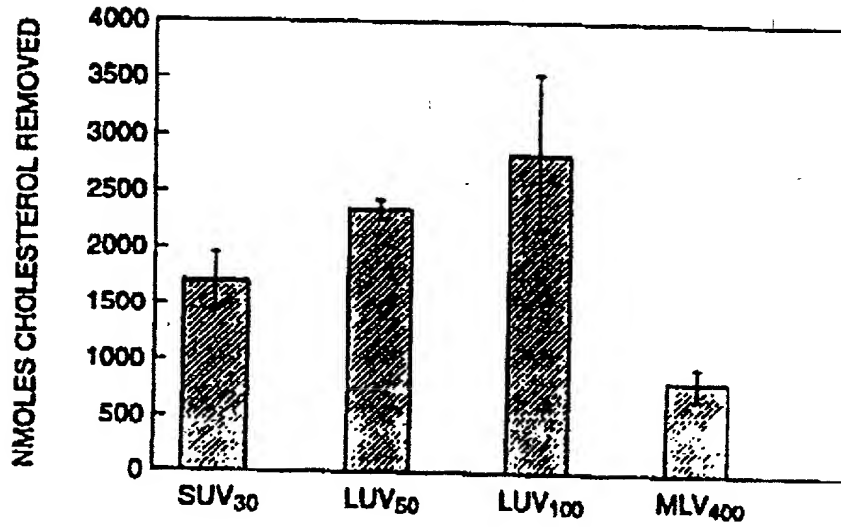


FIG. 35

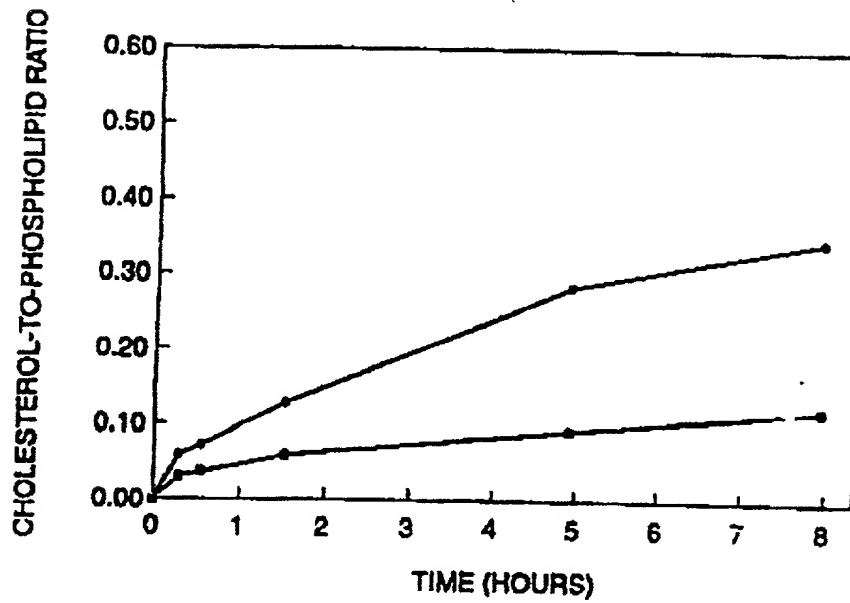


FIG. 36



33/40

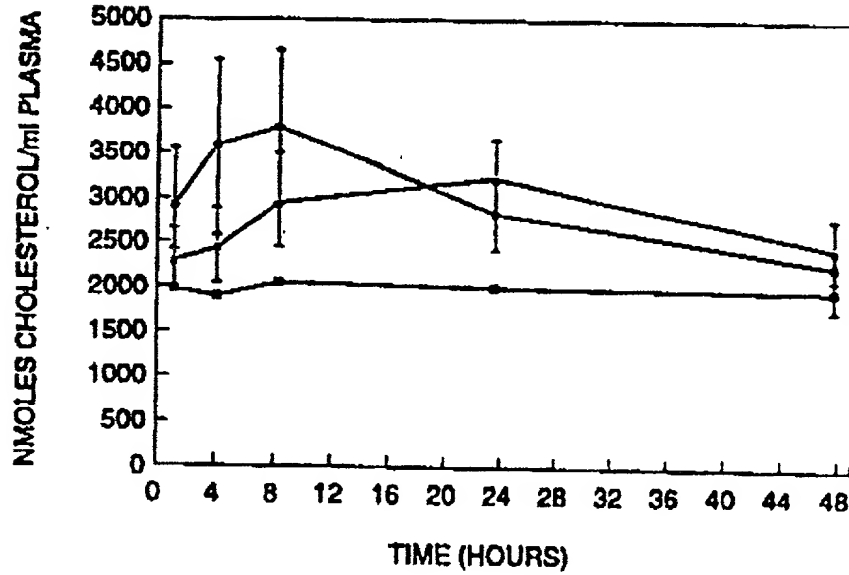


FIG. 37

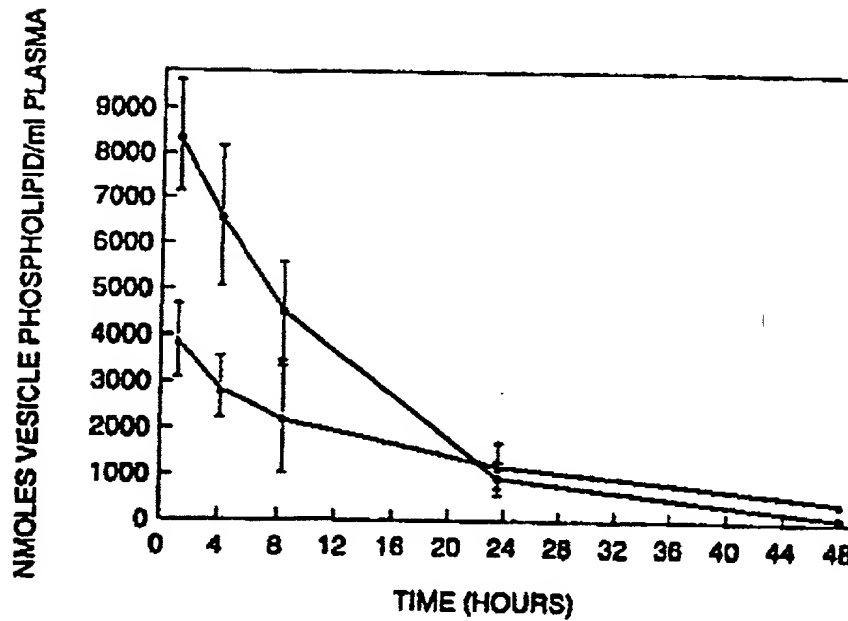


FIG. 38

34/40

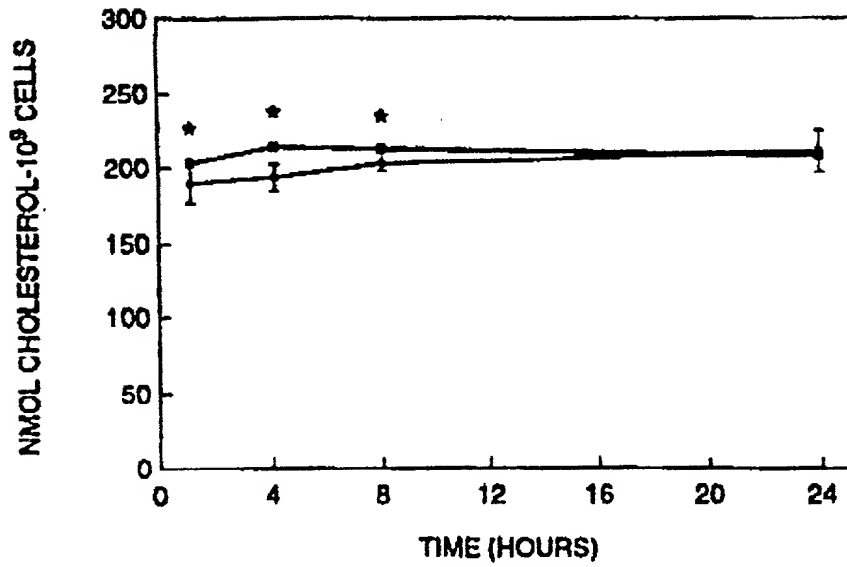


FIG. 39

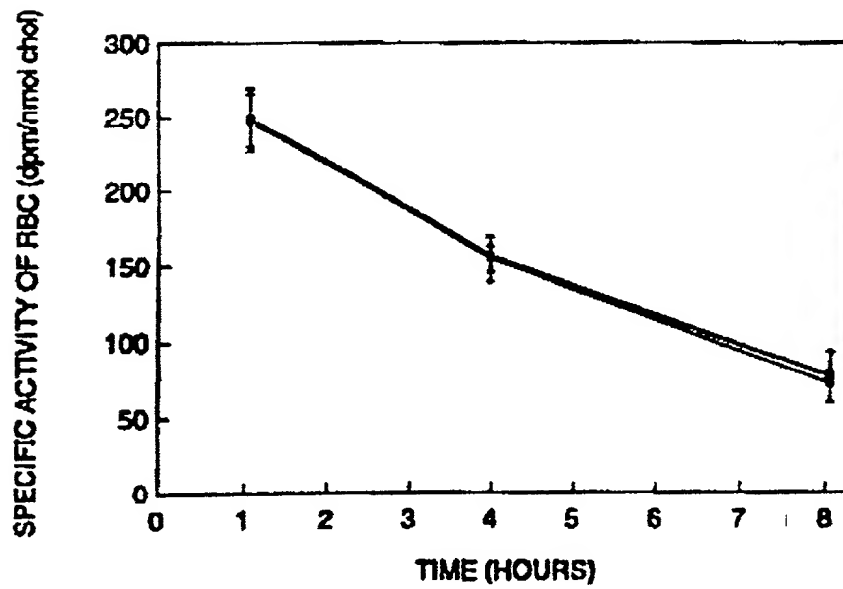


FIG. 40

35/40

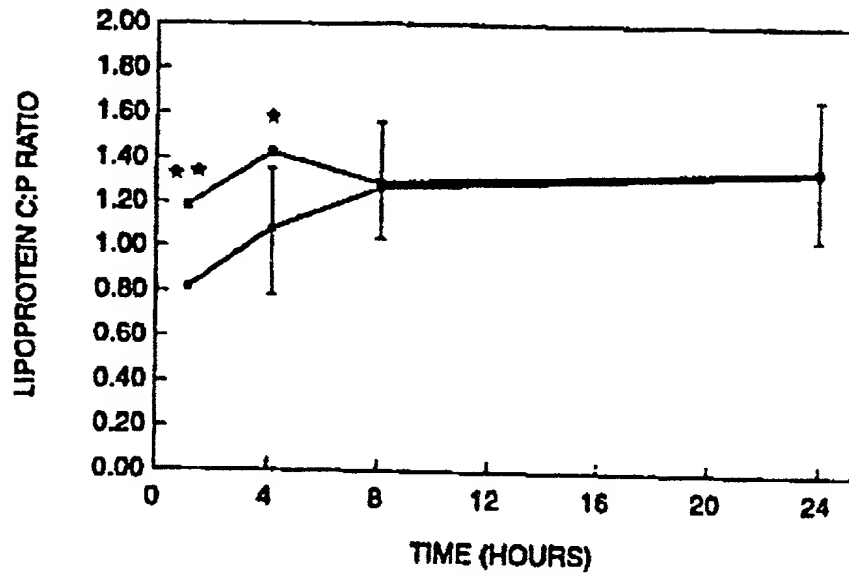


FIG. 41

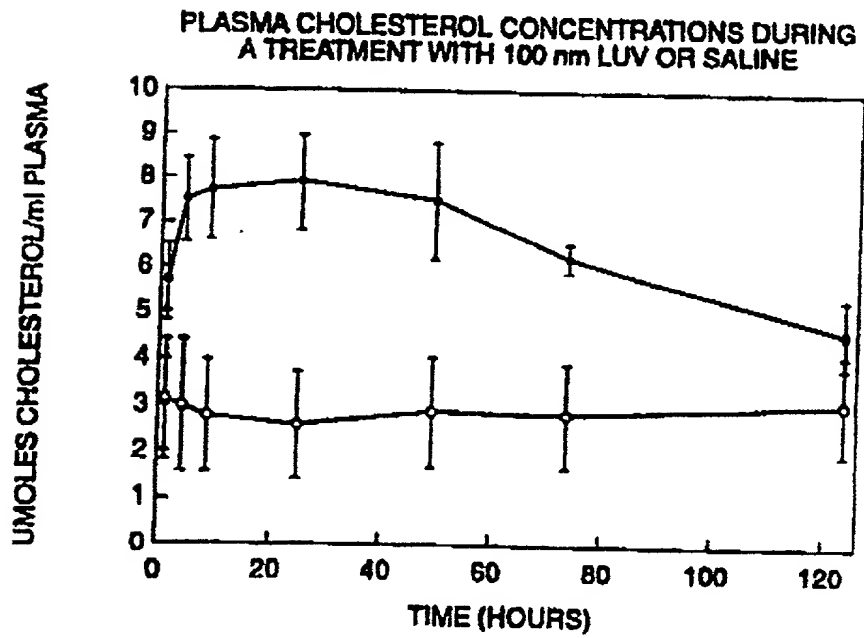


FIG. 42

36/40

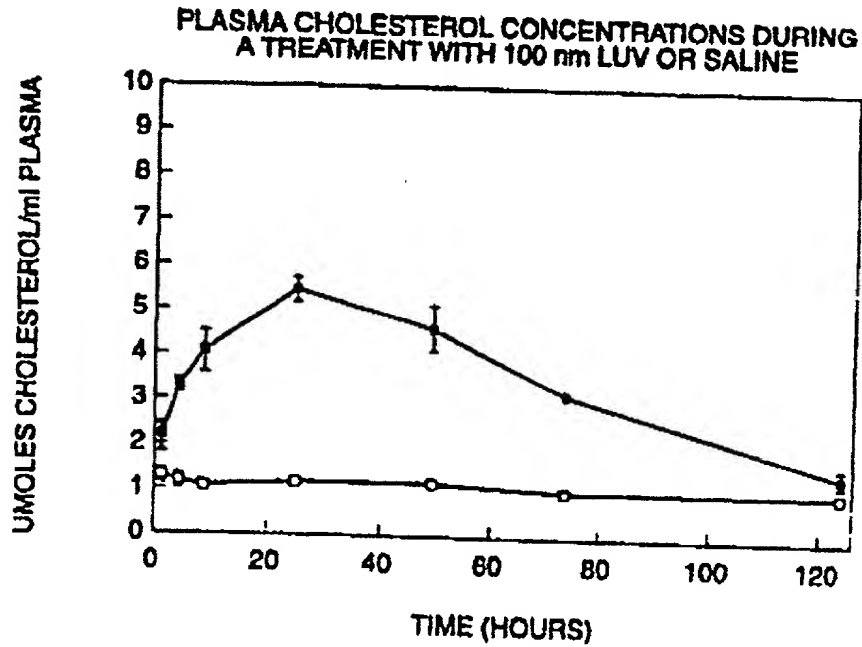


FIG. 43

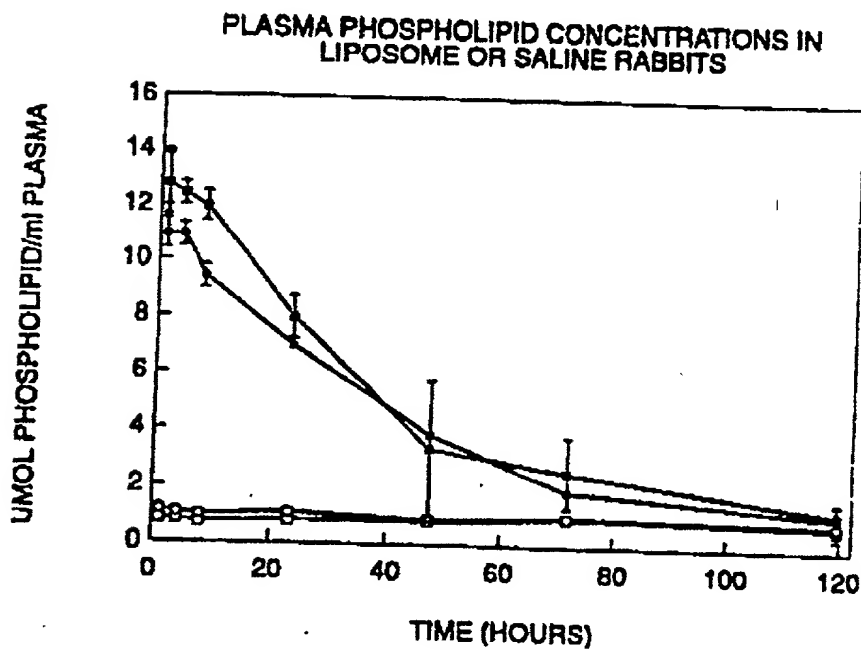


FIG. 44

37/40

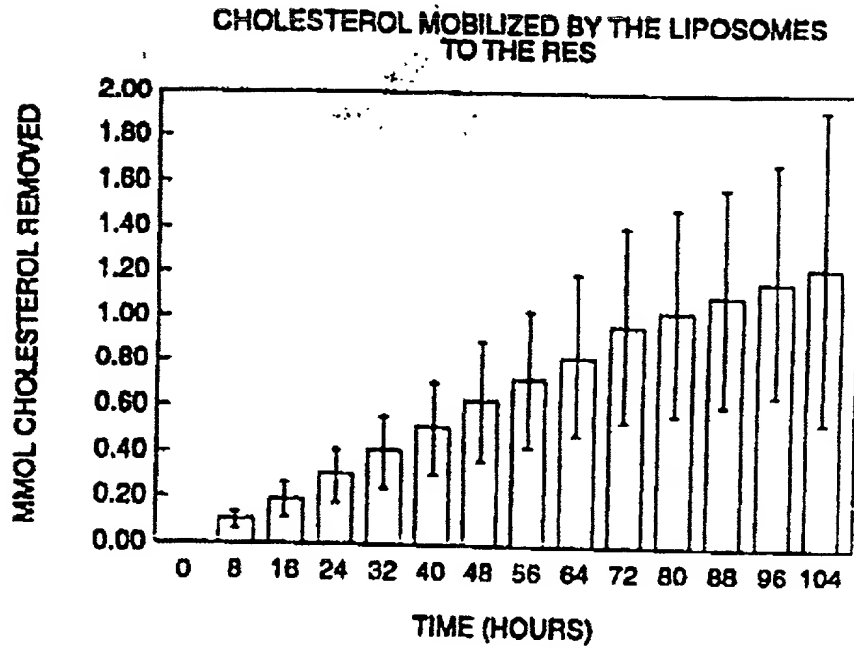


FIG. 45

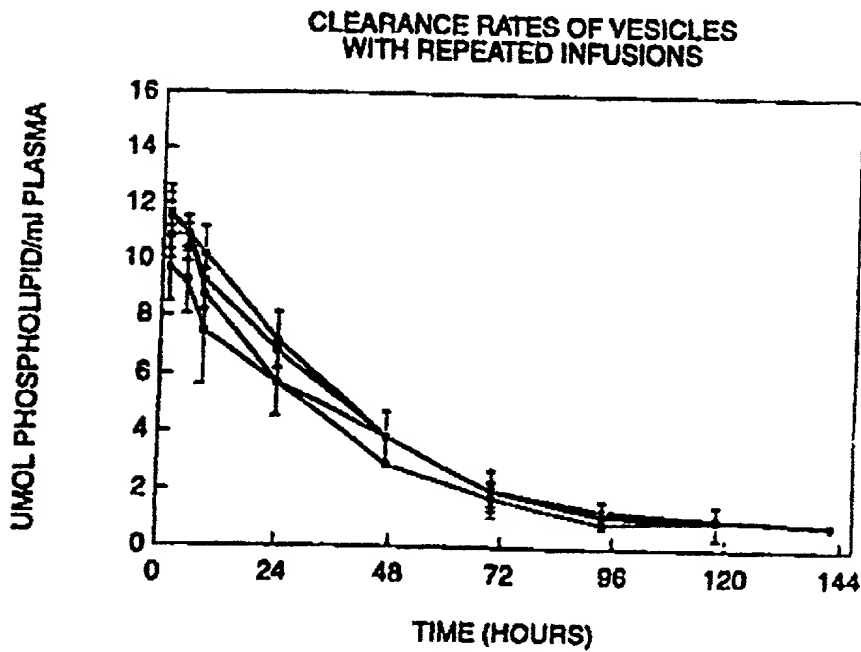


FIG. 46

38/40

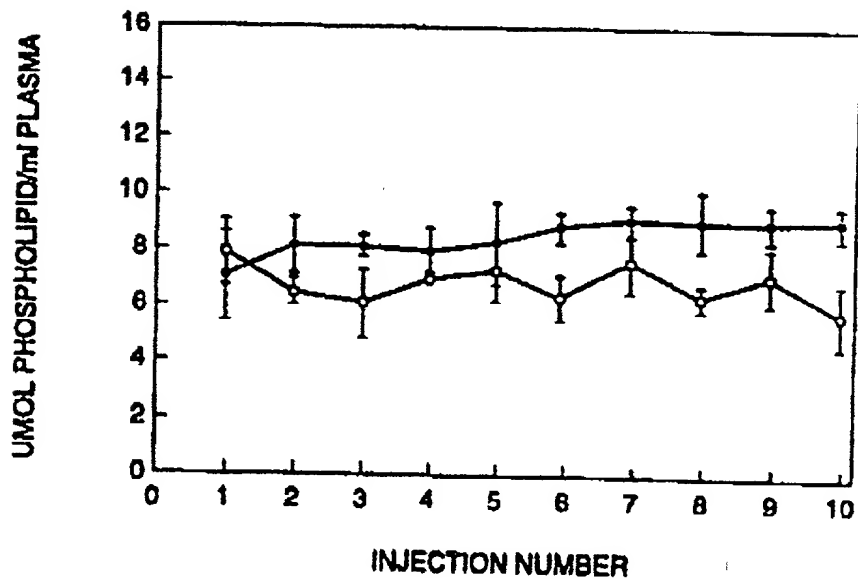


FIG. 47

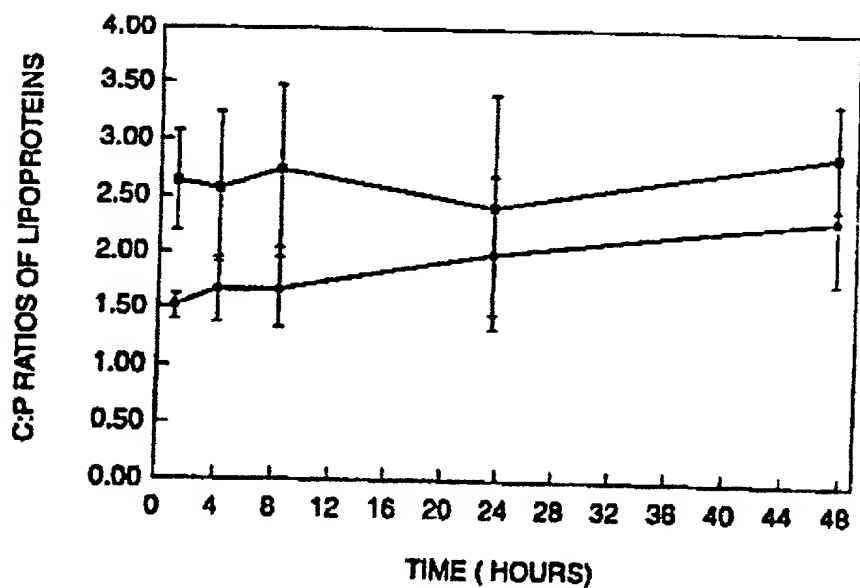


FIG. 48

39/40

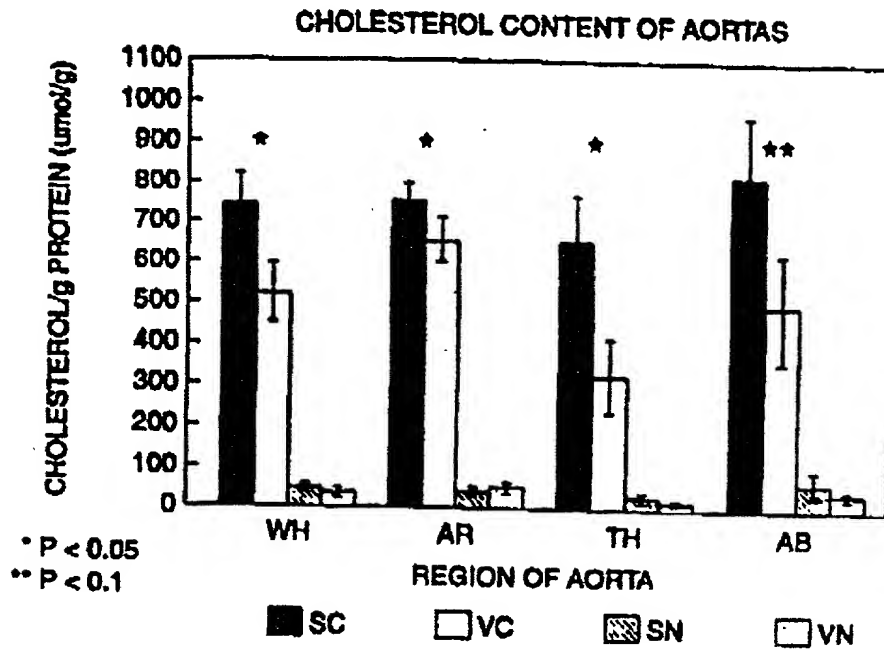


FIG. 49

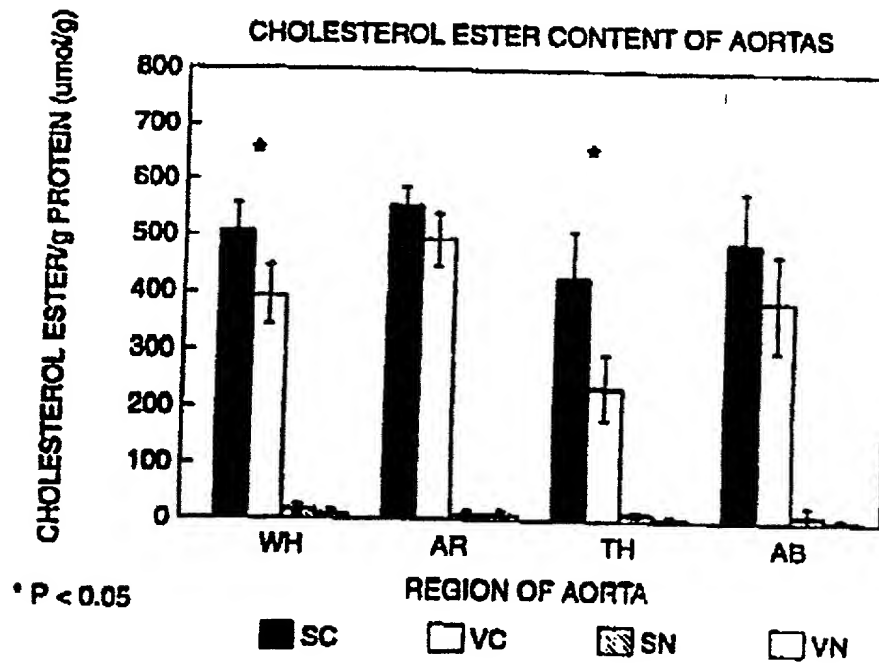


FIG. 50

40/40

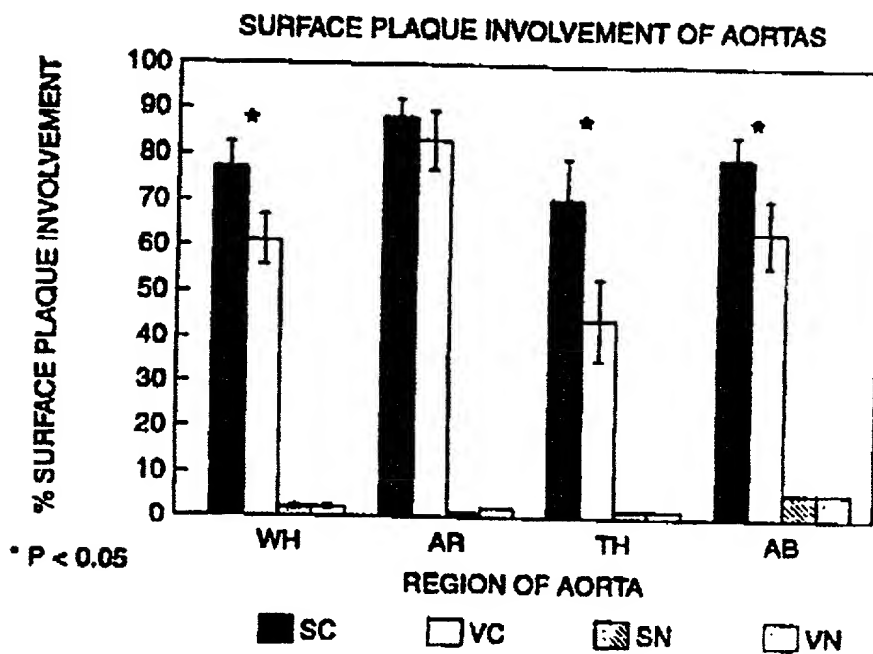


FIG. 51